# AMENDMENTS

**In the claims:**

Please amend Claim 2 so that it reads as follows.

2. (Amended) An isolated nucleic acid molecule comprising a nucleotide sequence that:

(a) encodes the amino acid sequence of SEQ ID NO:2; and

(b) hybridizes under highly stringent conditions including washing in 0.1xSSC/0.1% SDS at 68°C to the nucleotide sequence of SEQ ID NO: 1 or the complement thereof..

# RESPONSE

## I. Status of the Claims

Claim 2 has been amended. Claims 1, 2, 6 and 7 are therefore presently pending in the case. For the convenience of the Examiner, a clean copy of the pending claims is attached hereto as **Exhibit A**. In compliance with 37 C.F.R. § 1.121(c)(1)(ii), a marked up copy of the amended claims is attached hereto as **Exhibit B**.

## II. Support for the Amended Claims

Claim 2 has been amended to further clarify the claim, and to recite the specific highly stringent hybridization wash conditions described as an example in the specification. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least in Claim 2 as originally filed and at page 7, lines 32-35.

As the amendments to Claim 2 are fully supported by the specification and claims as originally filed, they do not constitute new matter. Entry therefore is respectfully requested.

## III. Rejection of Claims Under 35 U.S.C. §§ 101, 112, First Paragraph

Claims 1-2, 6 stand rejected, and new claim 7 is rejected, under 35 U.S.C. § 101 because they are drawn to an invention with no apparent or disclosed patentable utility, for reasons of record set forth in Paper No. 10, 7/1/02.

The Action disagrees with Applicants' logical assertion, based on the evidence, that the sequences of the present invention encode a novel human G-protein coupled receptor (GPCR) and that these molecules have a specific, credible, and well-established utility. The credibility of Applicants' assertion of credible and well-established utility of proteins that are structurally (7TM proteins) and functionally (G-protein interaction) related to the present sequences is evidenced by the fact that 60% of these drugs target G-protein coupled receptors (Gurrath, 2001, Curr. Med. Chem. *8*:1257-1299: **Exhibit C**). In addition, Applicants' assertion, that the presently described sequences have specific, credible and well-established utility, is also supported by the fact that multiple millions of dollars are allocated yearly in the identification and targeting of GPCRs, such as those of present invention. If these molecules did not have well-established utility recognized by those of skill in the art in the pharmaceutical industry, why would they direct so much of their limited resources to these molecules?

Given the legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable, this is clear evidence that those skilled in the art would have recognized the function and activity of the protein encoded by the sequences of the present invention, there can, therefore, be no question that Applicants' asserted utility for the described sequences is "credible." According to the Examination Guidelines for the Utility Requirement, if the applicant has asserted that the claimed invention is useful for any particular purpose (i.e., it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art, the Examiner should not impose a rejection based on lack of utility (66 Federal Register 1098, January 5, 2001).

Additionally, the real world utility of the present invention is clearly demonstrated by results obtained when a knockout mouse was made in which the mouse gene encoding the ortholog of SEQ ID NOS: 1 and 2 of the present invention was disrupted by homologous recombination. These knockout mice were subject to a medical work-up using an integrated suite of medical diagnostic procedures designed to assess the function of the major organ systems in a mammalian subject. Disruption of the mouse gene of the present invention and thus elimination of the protein it encodes,

resulted in neonatal lethality of the homozygous mutants, with 3 of the 9 homozygous(-/-) knockout mice born dying at approximately 1 day after birth. The remaining 6 homozygous(-/-)knockout mice exhibited muscle and limb control problems and died at 3 to 4 weeks of age. This provides evidence that the nucleic acid and protein encoded by the sequences of the present invention play an important role in the muscle and limb control processes. Clearly, such molecules, as well as agonists or antagonists directed at them, can be used to diagnose and treat muscle and limb control disorders and represent biologically validated drug targets. Therefore, without doubt the molecules of the present invention have real world substantial and specific utility.

The Action also discounts Applicants' assertion regarding the use of the presently claimed polynucleotides on DNA chips, based on the position that such a use would allegedly be generic. Further, the Action seems to be requiring Applicants to identify the biological role of the nucleic acid or function of the protein encoded by the presently claimed polynucleotides before the present sequences can be used in gene chip applications that meet the requirements of § 101. Applicants respectfully point out that knowledge of the exact function or role of the presently claimed sequence is not required to track expression patterns using a DNA chip. As set forth in Applicants First Response, given the widespread utility of such "gene chip" methods using *public domain* gene sequence information, there can be little doubt that the use of the presently described *novel* sequences would have great utility in such DNA chip applications. The claimed sequence provides a specific marker of the human genome (see evidence below), and that such specific markers are targets for discovering drugs that are associated with human disease. Thus, those skilled in the art would instantly recognize that the present nucleotide sequence would be an ideal, novel candidate for assessing gene expression using, for example, DNA chips, as the specification details. Such "DNA chips" clearly have utility, as evidenced by hundreds of issued U.S. Patents, as exemplified by U.S. Patent Nos. 5,445,934, 5,556,752, 5,744,305, as well as more recently issued U.S. Patent Nos. 5,837,832, 6,156,501 and 6,261,776. Accordingly, the present sequence has a specific utility in such DNA chip applications. Clearly, compositions that enhance the utility of such DNA chips, such as the presently claimed nucleotide sequence, must also be useful.

Furthermore, since only a small percentage of the genome (2-4%) actually encodes exons, which in-turn encode amino acid sequences. Thus, not all human genomic DNA sequences are useful in such gene chip applications, further discounting the Examiner's position that such uses are "generic".

Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101. It has been clearly established that a statement of utility in a specification must be accepted absent reasons why one skilled in the art would have reason to doubt the objective truth of such statement. *In re Langer*, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA, 1974); *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA, 1971).

In particular, as the molecules of the present invention have been shown to play a role in the control of muscle and limb processes, as evidenced in the knockout mice, clearly their use on "DNA chips" have specific and substantial utility.

Further evidence of utility of the presently claimed polynucleotide, although only one is needed to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), is the utility the present nucleotide sequence has a specific utility in determining the genomic structure of the corresponding human chromosome, for example mapping the protein encoding regions, as described in the specification and evidenced below. Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of the human chromosome containing the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequences (see evidence below). In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence.

Only a minor percentage of the genome actually encodes exons, which in-turn encode amino acid sequences. The presently claimed polynucleotide sequence provides biologically validated empirical data (*e.g.*, showing which sequences are transcribed, spliced, and polyadenylated) that *specifically* define that portion of the corresponding genomic locus that actually encodes exon sequence. Equally significant is that the claimed polynucleotide sequence defines how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon splice-junctions). Applicants respectfully submit that the practical

scientific value of expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts. For further evidence in support of the Applicants' position, the Board is requested to review, for example, section 3 of Venter *et al.* (*supra at* pp. 1317-1321, including Fig. 11 at pp.1324-1325), which demonstrates the significance of expressed sequence information in the structural analysis of genomic data. The presently claimed polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome essentially as described in the Venter *et al.* article.

As still further evidence supporting Applicants assertions of the specific utility of the sequences of the present invention in localizing the specific region of the human chromosome and identification of functionally active intron/exon splice junctions is the information provided in **Exhibit D**. This is the result of a blast analysis using SEQ ID NO:1 of the present invention when compared to the identified human genomic sequence. This result indicates that the sequence of the present invention is encoded by 25 exons spread non-contiguously along a region of human chromosome 6, which are contained within partially overlapping clones, AL360007.11 and AL033377.2. Thus clearly one would not simply be able to identify the 25 protein encoding exons that make up the sequence of the present intention from within the large genomic sequence. Nor, would one be able to map the protein encoding regions identified specifically by the sequences of the present invention without knowing exactly what those specific sequences were.

Finally, the Examiner has determined that applicants argument of due process presented in previous response is not persuasive. Applicants understanding is that issued United States patents retain a legal presumption of validity which in this case indicates that the inventions claimed in the cited patents are *legally presumed* to be in full compliance with the provisions of 35 U.S.C. sections 101, 102, 103, and 112. Applicants respectfully submit that, absent a change in the law as enacted by Congress and signed by the President, it is improper for the Examiner to hold Applicants' invention to a different legal standard of patentability. Given the rapid pace of development in the biotechnology arts, it is difficult for the Applicants to understand how an invention fully disclosed and free of prior art at the time the present application was filed, could somehow retain *less* utility and be *less* enabled than inventions in the cited issued U.S. patents (which were filed during a time when the level of skill in the art was clearly lower). Simply put, Applicants invention is *more* enabled and retains *at least as much* utility as the inventions described in the claims of the U.S. patents of record. Any argument to the

contrary is at best arbitrary and at worst capricious. Absent authority provided by an act of Congress or Executive order, arbitrary or capricious conduct by an administrative office the U.S. government has historically proven to conflict with the provisions of the U.S. Constitution. The Patent Office does not have the authority to rewrite U.S. law. However, the Patent Office does have a Constitutional obligation to administer U.S. law in an unbiased and procedurally consistent manner. That is what the Applicants are respectfully requesting the Examiner to consider in the present matter.

For each of the foregoing reasons, Applicants submit that in light of the above discussion and those presented in previous Applicant responses, the presently claimed invention has been shown to have a substantial, specific, credible and well-established utility and that the rejection of pending claims 1-5 under 35 U.S.C. § 101 has been avoided, and respectfully request that the rejection be withdrawn.

## IV. Rejection of Claims Under 35 U.S.C. § 112, First Paragraph

The Action rejects claims 1, 2 and 6 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by a specific, substantial, and credible utility or a well-established utility. Applicants respectfully traverse.

As demonstrated extensively in the section above, the present invention is supported by a specific, substantial, credible and well-established utility. The function of the protein encoded by the sequences of the present invention is that of a GPCR involved in muscle and limb control. Thus, Applicants submit that as the claims have been shown to have a specific, substantial, credible and well established utility, as detailed in the section above, Applicants respectfully request that the rejection of claims 1,2,6 and 7 under 35 U.S.C. § 112, first paragraph, be withdrawn.

## V. Rejection of Claims Under 35 U.S.C. § 112, Second Paragraph

Claim 2 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants respectfully disagree. While Applicants submit that the term is sufficiently definite, as a number of stringent hybridization conditions are defined in the specification and would be known to those of skill in the art, solely in order to progress the case more rapidly toward allowance the claim

has been revised to recite the exact hybridization wash conditions described as an example in the specification as originally filed. Applicants submit that revised Claim 2 even more clearly meets the requirements of 35 U.S.C. § 112, second paragraph. Applicants stress that "a claim need not 'describe' the invention, such description being the role of the disclosure". *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986). Based on the foregoing, Applicants submit that Claim 2 is sufficiently definite, and respectfully request withdrawal of this rejection.

## VI. Conclusion

The present document is a full and complete response to the Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case are now in condition for allowance, and such favorable action is respectfully requested. Should Examiner Murphy have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

This response is timely filed and Applicants believe no fees are due in connection with this response. However, should this be incorrect the Commissioner is authorized to charge any required fees or credit any overpayment to Deposit Account No. 50-0892.

Respectfully submitted,

April 28, 2003
Date

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**Exhibit A**

**Clean Version of The Pending Claims in U.S. Patent Application Ser. No. 09/658,283**

1.(previously amended) An isolated nucleic acid molecule containing the nucleotide sequence described in SEQ ID NO: 1.

2.(twice amended) An isolated nucleic acid molecule comprising a nucleotide sequence that:

(a) encodes the amino acid sequence shown in SEQ ID NO: 2; and

(b) hybridizes under highly stringent conditions including washing in 0.1xSSC/0.1% SDS at 68°C to the nucleotide sequence of SEQ ID NO: 1 or the complement thereof.

6.(original) An expression vector comprising an isolated polynucleotide encoding the amino acid sequence presented in SEQ ID NO: 2.

7.(previously added) A cell comprising the expression vector of Claim 6.